

SEQUENCE LISTING

<110> Borean Pharma A/S

JC20 Rec'd PCT/PTO 21 OCT 2005

<120> Cleavage of fusion proteins using Granzyme B protease

<130> 3106

<160> 57

<170> PatentIn version 3.2

<210> 1

<211> 243

<212> PRT

<213> Artificial

<220>

<223> pro-IEGR-GrB-H6

<400> 1

Met Gly Ser Ile Glu Gly Arg Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

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<400> 2

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

<210> 3
<211> 243
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<213> Artificial

<220>
<223> pro-IEAD-GrB-H6

<400> 3

Met Gly Ser Ile Glu Ala Asp Ile Ile Gly Gly His Glu Ala Lys Pro

1	5	10	15																
His	Ser	Arg	Pro	Tyr	Met	Ala	Tyr	Leu	Met	Ile	Trp	Asp	Gln	Lys	Ser				
			20					25					30						
Leu	Lys	Arg	Cys	Gly	Gly	Phe	Leu	Ile	Gln	Asp	Asp	Phe	Val	Leu	Thr				
		35					40					45							
Ala	Ala	His	Cys	Trp	Gly	Ser	Ser	Ile	Asn	Val	Thr	Leu	Gly	Ala	His				
	50					55					60								
Asn	Ile	Lys	Glu	Gln	Glu	Pro	Thr	Gln	Gln	Phe	Ile	Pro	Val	Lys	Arg				
65					70					75					80				
Pro	Ile	Pro	His	Pro	Ala	Tyr	Asn	Pro	Lys	Asn	Phe	Ser	Asn	Asp	Ile				
			85					90						95					
Met	Leu	Leu	Gln	Leu	Glu	Arg	Lys	Ala	Lys	Arg	Thr	Arg	Ala	Val	Gln				
			100					105					110						
Pro	Leu	Arg	Leu	Pro	Ser	Asn	Lys	Ala	Gln	Val	Lys	Pro	Gly	Gln	Thr				
		115					120					125							
Cys	Ser	Val	Ala	Gly	Trp	Gly	Gln	Thr	Ala	Pro	Leu	Gly	Lys	His	Ser				
	130					135					140								
His	Thr	Leu	Gln	Glu	Val	Lys	Met	Thr	Val	Gln	Glu	Asp	Arg	Lys	Cys				
145					150					155					160				
Glu	Ser	Asp	Leu	Arg	His	Tyr	Tyr	Asp	Ser	Thr	Ile	Glu	Leu	Cys	Val				
				165					170					175					
Gly	Asp	Pro	Glu	Ile	Lys	Lys	Thr	Ser	Phe	Lys	Gly	Asp	Ser	Gly	Gly				
		180						185					190						
Pro	Leu	Val	Cys	Asn	Lys	Val	Ala	Gln	Gly	Ile	Val	Ser	Tyr	Gly	Arg				
		195					200					205							
Asn	Asn	Gly	Met	Pro	Pro	Arg	Ala	Cys	Thr	Lys	Val	Ser	Ser	Phe	Val				
	210					215					220								
His	Trp	Ile	Lys	Lys	Thr	Met	Lys	Arg	Tyr	Leu	Asn	Ser	His	His	His				
225					230					235					240				

His His His

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<213> Artificial

<220>
<223> pro-IEPD-GrB-H6 C228S

<400> 4

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val

	165		170		175
Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly					
	180		185		190
Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg					
	195		200		205
Asn Asn Gly Met Pro Pro Arg Ala Ser Thr Lys Val Ser Ser Phe Val					
	210		215		220
His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His					
	225		230		235
					240

His His His

<210> 5
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Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro	
1 5 10 15	
His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser	
20 25 30	
Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr	
35 40 45	
Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His	
50 55 60	
Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg	
65 70 75 80	
Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile	
85 90 95	

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Ala Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 6
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 <212> PRT
 <213> Artificial

<220>
 <223> pro-IEPD-GrB-H6 C228T

<400> 6

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Thr Thr Lys Val Ser Ser Phe Val
210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
225 230 235 240

His His His

<210> 7
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 <213> Artificial

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 <223> pro-IEPD-GrB-H6 C228V

<400> 7

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Val Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 8
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 <223> pro-IEPD-GrB-H6 C228F

<400> 8

Met Gly Ser Ile Glu Pro Asp Ile Ile Gly Gly His Glu Ala Lys Pro
 1 5 10 15

His Ser Arg Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser
 20 25 30

Leu Lys Arg Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr
 35 40 45

Ala Ala His Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His
 50 55 60

Asn Ile Lys Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg
 65 70 75 80

Pro Ile Pro His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile
 85 90 95

Met Leu Leu Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln
 100 105 110

Pro Leu Arg Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr
 115 120 125

Cys Ser Val Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser
 130 135 140

His Thr Leu Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys
 145 150 155 160

Glu Ser Asp Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val
 165 170 175

Gly Asp Pro Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly
 180 185 190

Pro Leu Val Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg
 195 200 205

Asn Asn Gly Met Pro Pro Arg Ala Phe Thr Lys Val Ser Ser Phe Val
 210 215 220

His Trp Ile Lys Lys Thr Met Lys Arg Tyr Leu Asn Ser His His His
 225 230 235 240

His His His

<210> 9
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 <212> DNA
 <213> Artificial

<220>
 <223> H6 C-term fw

<400> 9
 catggacgga agcttgaatt cacatcacca tcaccatcac taacgc

46

<210> 10
 <211> 46
 <212> DNA
 <213> Artificial

<220>
 <223> H6 C-term rev

<400> 10
 aattgcgtta gtgatggtga tggatgatgtg aattcaagct tccgct

46

<210> 11
 <211> 40
 <212> DNA
 <213> Artificial

 <220>
 <223> GrBfw primer

 <400> 11
 catgggatcc atcgagggtg ggatcatcgg gggacatgag 40

 <210> 12
 <211> 38
 <212> DNA
 <213> Artificial

 <220>
 <223> GrBrev EcoRI primer

 <400> 12
 gcgtgaattc aggtaccgtt tcatggtttt ctttatcc 38

 <210> 13
 <211> 715
 <212> DNA
 <213> Artificial

 <220>
 <223> GrB EcoRI fragment

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 ctacatggct tatcttatga tctgggatca gaagtctctg aagagggtgcg gtggcttcct 120
 gatacaagac gacttcgtgc tgacagctgc tctactgttg ggaagctcca taaatgtcac 180
 cttggggggcc cacaatatca aagaacagga gccgaccag cagtttatcc ctgtgaaaag 240
 acccatcccc catccagcct ataatcctaa gaacttctcc aacgacatca tgctactgca 300
 gctggagaga aaggccaagc ggaccagagc tgtgcagccc cttaggctac ctagcaacaa 360
 ggcccagggtg aagccagggc agacatgcag tgtggccggc tgggggcaga cggccccct 420
 gggaaaacac tcacacacac tacaagaggt gaagatgaca gtgcaggaag atcgaaagtg 480
 cgaatctgac ttacgccatt attacgacag taccattgag ttgtgctggg gggaccaga 540
 gattaataaag acttccttta agggggactc tggaggccct cttgtgtgta acaagggtggc 600
 ccagggcatt gtctcctatg gacgaaacaa tggcatgcct ccacgagcct gcaccaaagt 660
 ctcaagcttt gtacactgga taaagaaaac catgaaacgg tacctgaatt cacgc 715

<210> 14
 <211> 33
 <212> DNA
 <213> Artificial

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 <223> GrB GR-PD fw

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 tccatcgagc cggatatcat cgggggacat gag 33

 <210> 15
 <211> 34
 <212> DNA
 <213> Artificial

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 <223> GrB GR-PD rev

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 ccccgatgat atccggctcg atggatccca tatg 34

 <210> 16
 <211> 33
 <212> DNA
 <213> Artificial

 <220>
 <223> GrB GR-AD fw

 <400> 16
 tccatcgagg ctgatcat cgggggacat gag 33

 <210> 17
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> GrB GR-AD rev

 <400> 17
 ccccgatgat atcagcctcg atggatccca tatg 34

 <210> 18
 <211> 27
 <212> DNA
 <213> Artificial

 <220>
 <223> GrB SAT fw

<400> 18
tccacgagca dccaccaaag tctcaag 27

<210> 19
<211> 26
<212> DNA
<213> Artificial

<220>
<223> GrB SAT rev

<400> 19
agactttggt gghggctcgt ggaggc 26

<210> 20
<211> 27
<212> DNA
<213> Artificial

<220>
<223> GrB VF fw

<400> 20
tccacgagcc ktcaccaaag tctcaag 27

<210> 21
<211> 26
<212> DNA
<213> Artificial

<220>
<223> GrB VF rev

<400> 21
agactttggt gamggctcgt ggaggc 26

<210> 22
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!SP

<400> 22

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
 35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
 50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
 65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
 85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
 100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser
 145 150

<210> 23
 <211> 338
 <212> PRT
 <213> Artificial

<220>
 <223> H6-IEPD-RAP

<400> 23

Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Tyr
 1 5 10 15

Ser Arg Glu Lys Asn Gln Pro Lys Pro Ser Pro Lys Arg Glu Ser Gly
 20 25 30

Glu Glu Phe Arg Met Glu Lys Leu Asn Gln Leu Trp Glu Lys Ala Gln
 35 40 45

Arg Leu His Leu Pro Pro Val Arg Leu Ala Glu Leu His Ala Asp Leu

50					55					60					
Lys 65	Ile	Gln	Glu	Arg	Asp 70	Glu	Leu	Ala	Trp	Lys 75	Lys	Leu	Lys	Leu	Asp 80
Gly	Leu	Asp	Glu	Asp 85	Gly	Glu	Lys	Glu	Ala 90	Arg	Leu	Ile	Arg	Asn 95	Leu
Asn	Val	Ile	Leu 100	Ala	Lys	Tyr	Gly	Leu 105	Asp	Gly	Lys	Lys	Asp 110	Ala	Arg
Gln	Val	Thr 115	Ser	Asn	Ser	Leu	Ser 120	Gly	Thr	Gln	Glu	Asp 125	Gly	Leu	Asp
Asp 130	Pro	Arg	Leu	Glu	Lys	Leu 135	Trp	His	Lys	Ala	Lys 140	Thr	Ser	Gly	Lys
Phe 145	Ser	Gly	Glu	Glu 150	Leu	Asp	Lys	Leu	Trp	Arg 155	Glu	Phe	Leu	His 160	His
Lys	Glu	Lys	Val 165	His	Glu	Tyr	Asn	Val 170	Leu	Leu	Glu	Thr	Leu	Ser 175	Arg
Thr	Glu	Glu	Ile 180	His	Glu	Asn	Val 185	Ile	Ser	Pro	Ser	Asp	Leu	Ser	Asp
Ile	Lys	Gly 195	Ser	Val	Leu	His	Ser 200	Arg	His	Thr	Glu	Leu 205	Lys	Glu	Lys
Leu 210	Arg	Ser	Ile	Asn	Gln 215	Gly	Leu	Asp	Arg	Leu	Arg 220	Arg	Val	Ser	His
Gln 225	Gly	Tyr	Ser	Thr 230	Glu	Ala	Glu	Phe	Glu	Glu 235	Pro	Arg	Val	Ile	Asp 240
Leu	Trp	Asp	Leu	Ala 245	Gln	Ser	Ala	Asn	Leu	Thr 250	Asp	Lys	Glu	Leu 255	Glu
Ala	Phe	Arg	Glu 260	Glu	Leu	Lys	His	Phe 265	Glu	Ala	Lys	Ile	Glu 270	Lys	His
Asn	His	Tyr 275	Gln	Lys	Gln	Leu	Glu 280	Ile	Ala	His	Glu	Lys 285	Leu	Arg	His

Ala Glu Ser Val Gly Asp Gly Glu Arg Val Ser Arg Ser Arg Glu Lys
 290 295 300

His Ala Leu Leu Glu Gly Arg Thr Lys Glu Leu Gly Tyr Thr Val Lys
 305 310 315 320

Lys His Leu Gln Asp Leu Ser Gly Arg Ile Ser Arg Ala Arg His Asn
 325 330 335

Glu Leu

<210> 24
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 <212> PRT
 <213> Artificial

<220>
 <223> H6Ubi-IEPD-ApoA1

<400> 24

Met Gly Ser His His His His His His Gly Ser Gln Ile Phe Val Lys
 1 5 10 15

Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr
 20 25 30

Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro
 35 40 45

Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg
 50 55 60

Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val
 65 70 75 80

Leu Arg Leu Arg Gly Gly Ser Ile Glu Pro Asp Gly Gly Asp Glu Pro
 85 90 95

Pro Gln Ser Pro Trp Asp Arg Val Lys Asp Leu Ala Thr Val Tyr Val
 100 105 110

Asp Val Leu Lys Asp Ser Gly Arg Asp Tyr Val Ser Gln Phe Glu Gly

115	120	125
Ser Ala Leu Gly Lys Gln Leu Asn Leu Lys Leu Leu Asp Asn Trp Asp 130 135 140		
Ser Val Thr Ser Thr Phe Ser Lys Leu Arg Glu Gln Leu Gly Pro Val 145 150 155 160		
Thr Gln Glu Phe Trp Asp Asn Leu Glu Lys Glu Thr Glu Gly Leu Arg 165 170 175		
Gln Glu Met Ser Lys Asp Leu Glu Glu Val Lys Ala Lys Val Gln Pro 180 185 190		
Tyr Leu Asp Asp Phe Gln Lys Lys Trp Gln Glu Glu Met Glu Leu Tyr 195 200 205		
Arg Gln Lys Val Glu Pro Leu Arg Ala Glu Leu Gln Glu Gly Ala Arg 210 215 220		
Gln Lys Leu His Glu Leu Gln Glu Lys Leu Ser Pro Leu Gly Glu Glu 225 230 235 240		
Met Arg Asp Arg Ala Arg Ala His Val Asp Ala Leu Arg Thr His Leu 245 250 255		
Ala Pro Tyr Ser Asp Glu Leu Arg Gln Arg Leu Ala Ala Arg Leu Glu 260 265 270		
Ala Leu Lys Glu Asn Gly Gly Ala Arg Leu Ala Glu Tyr His Ala Lys 275 280 285		
Ala Thr Glu His Leu Ser Thr Leu Ser Glu Lys Ala Lys Pro Ala Leu 290 295 300		
Glu Asp Leu Arg Gln Gly Leu Leu Pro Val Leu Glu Ser Phe Lys Val 305 310 315 320		
Ser Phe Leu Ser Ala Leu Glu Glu Tyr Thr Lys Lys Leu Asn Thr Gln 325 330 335		

<210> 25
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<212> PRT
<213> Artificial

<220>

<223> H6-IEPD-TN123

<400> 25

Met Gly Ser His His His His His His Gly Ser Ile Glu Pro Asp Gly
1 5 10 15

Glu Pro Pro Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
20 25 30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
35 40 45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
50 55 60

Val Cys Leu Lys Gly Thr Lys Val His Met Lys Cys Phe Leu Ala Phe
65 70 75 80

Thr Gln Thr Lys Thr Phe His Glu Ala Ser Glu Asp Cys Ile Ser Arg
85 90 95

Gly Gly Thr Leu Ser Thr Pro Gln Thr Gly Ser Glu Asn Asp Ala Leu
100 105 110

Tyr Glu Tyr Leu Arg Gln Ser Val Gly Asn Glu Ala Glu Ile Trp Leu
115 120 125

Gly Leu Asn Asp Met Ala Ala Glu Gly Thr Trp Val Asp Met Thr Gly
130 135 140

Ala Arg Ile Ala Tyr Lys Asn Trp Glu Thr Glu Ile Thr Ala Gln Pro
145 150 155 160

Asp Gly Gly Lys Thr Glu Asn Cys Ala Val Leu Ser Gly Ala Ala Asn
165 170 175

Gly Lys Trp Phe Asp Lys Arg Cys Arg Asp Gln Leu Pro Tyr Ile Cys
180 185 190

Gln Phe Gly Ile Val

195

<210> 26
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IQAD!SP

<400> 26

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 27
<211> 150
<212> PRT
<213> Artificial

<220>

<223> H6-TripUB IQAD!SG

<400> 27

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Gln Ala Asp Ser Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 28

<211> 150

<212> PRT

<213> Artificial

<220>

<223> H6-TripUB VGPD!SP

<400> 28

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val

1 5 10 15

Gly Pro Asp Ser Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 29
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB VGPD!FG

<400> 29

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Val
1 5 10 15

Gly Pro Asp Phe Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
 35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
 50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
 65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
 85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
 100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser
 145 150

<210> 30
 <211> 143
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!TQ

<400> 30

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Thr Gln Lys Pro Lys Lys Ile Val Asn Ala Lys Lys Asp
 20 25 30

Val Val Asn Thr Lys Met Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr
 35 40 45

Leu Ala Gln Glu Val Ala Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr
 50 55 60

Val Gly Ser Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
65 70 75 80

Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
85 90 95

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
100 105 110

Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
115 120 125

Lys Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ser
130 135 140

<210> 31
<211> 137
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!IV

<400> 31

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met
20 25 30

Phe Glu Glu Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala
35 40 45

Leu Leu Lys Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe
50 55 60

Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser
65 70 75 80

Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile
85 90 95

Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp
100 105 110

Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His
 115 120 125

Leu Val Leu Arg Leu Arg Gly Gly Ser
 130 135

<210> 32
 <211> 150
 <212> PRT
 <213> Artificial

<220>
 <223> H6-TripUB IEPD!EP

<400> 32

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
 1 5 10 15

Glu Pro Asp Glu Pro Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
 20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
 35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
 50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
 65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
 85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
 100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
 115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
 130 135 140

Arg Leu Arg Gly Gly Ser

145

150

<210> 33
<211> 150
<212> PRT
<213> Artificial

<220>
<223> H6-TripUB IEPD!EG

<400> 33

Met Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser Ile
1 5 10 15

Glu Pro Asp Glu Gly Gly Thr Glu Pro Pro Thr Gln Lys Pro Lys Lys
20 25 30

Ile Val Asn Ala Lys Lys Asp Val Val Asn Thr Lys Met Phe Glu Glu
35 40 45

Leu Lys Ser Arg Leu Asp Thr Leu Ala Gln Glu Val Ala Leu Leu Lys
50 55 60

Glu Gln Gln Ala Leu Gln Thr Val Gly Ser Gln Ile Phe Val Lys Thr
65 70 75 80

Leu Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile
85 90 95

Glu Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp
100 105 110

Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr
115 120 125

Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu
130 135 140

Arg Leu Arg Gly Gly Ser
145 150

<210> 34
<211> 37
<212> DNA
<213> Artificial

<220>
 <223> TripUB GrB fw primer

 <400> 34
 gtggatccat cgagcctgac tctcctggta ccgagcc 37

 <210> 35
 <211> 38
 <212> DNA
 <213> Artificial

 <220>
 <223> TripUB GrB rev primer

 <400> 35
 ggtaccagga gagtcaggct cgatggatcc actaccac 38

 <210> 36
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> RAP GrB fw primer

 <400> 36
 cggatccatc gagcctgact actcgcggga gaag 34

 <210> 37
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> RAP GrB rev primer

 <400> 37
 cccgcgagta gtcaggctcg atggatccgt gatg 34

 <210> 38
 <211> 42
 <212> DNA
 <213> Artificial

 <220>
 <223> Mut-GrB fw

 <400> 38
 cgtggtggat ccatcgagcc ggacggtgga gatgaacccc cc 42

 <210> 39

<211> 42
 <212> DNA
 <213> Artificial

 <220>
 <223> Mut-GrB rw

 <400> 39
 ggggggttca tctccaccgt ccggctcgat ggatccacca cg 42

 <210> 40
 <211> 33
 <212> DNA
 <213> Artificial

 <220>
 <223> TN GrB fw primer

 <400> 40
 ggatccatcg agcctgacgg cgagccacca acc 33

 <210> 41
 <211> 33
 <212> DNA
 <213> Artificial

 <220>
 <223> TN GrB rev primer

 <400> 41
 ggctcgccgt caggctcgat ggatccgtga tgg 33

 <210> 42
 <211> 33
 <212> DNA
 <213> Artificial

 <220>
 <223> PC7TripUB GR-AD fw

 <400> 42
 ggatccatcc aggcagactc tcttggtacc gag 33

 <210> 43
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> PC7TripUB GR-AD rev

 <400> 43
 gtaccaggag agtctgcctg gatggatcca ctac 34

<210> 44
 <211> 37
 <212> DNA
 <213> Artificial

 <220>
 <223> PC7TripUB P-G fw

 <400> 44
 ggatccatcc aggcagactc tgggtggtacc gagccac 37

 <210> 45
 <211> 38
 <212> DNA
 <213> Artificial

 <220>
 <223> PC7TripUB P-G rev

 <400> 45
 ctcggtacca ccagagtctg cctggatgga tccactac 38

 <210> 46
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> DNATrip IE-VG fw

 <400> 46
 gtagtggatc agtcgggcct gactctcctg gtac 34

 <210> 47
 <211> 34
 <212> DNA
 <213> Artificial

 <220>
 <223> DNATrip IE-VG rev

 <400> 47
 gagagtcagg cccgactgat ccactaccac tacc 34

 <210> 48
 <211> 31
 <212> DNA
 <213> Artificial

 <220>
 <223> DNATrip SP-FG fw

<400> 48
 ggctgactt tgggtggtacc gagccaccaa c 31

<210> 49
 <211> 31
 <212> DNA
 <213> Artificial

<220>
 <223> DNATrip SP-FG rev

<400> 49
 ggctcggtac \caccaaagtc aggcccgact g 31

<210> 50
 <211> 52
 <212> DNA
 <213> Artificial

<220>
 <223> Trip IEPD-TQ

<400> 50
 gggaaaggat ccatcgagcc tgacaccag aagcccaaga agattgtaaa tg 52

<210> 51
 <211> 54
 <212> DNA
 <213> Artificial

<220>
 <223> Trip IEPD-IV

<400> 51
 gggaaaggat ccatcgagcc tgacattgta aatgcccaaga aagatgttgt gaac 54

<210> 52
 <211> 39
 <212> DNA
 <213> Artificial

<220>
 <223> UB3

<400> 52
 cgcaagcttg catgottagg atccaccag aagtctcaa 39

<210> 53
 <211> 29
 <212> DNA
 <213> Artificial

<220>
 <223> TripUB EP fw

 <400> 53
 cgagcctgac gagcctggta ccgagccac 29

 <210> 54
 <211> 30
 <212> DNA
 <213> Artificial

 <220>
 <223> TripUB EP rev

 <400> 54
 cgggtaccagg ctcgtcaggc tcgatggatc 30

 <210> 55
 <211> 29
 <212> DNA
 <213> Artificial

 <220>
 <223> TripUB EG fw

 <400> 55
 cctgacgagg gtggtaccga gccaccaac 29

 <210> 56
 <211> 29
 <212> DNA
 <213> Artificial

 <220>
 <223> TripUB EG rev

 <400> 56
 gctcggtacc accctcgta ggctcgatg 29

 <210> 57
 <211> 227
 <212> PRT
 <213> Artificial

 <220>
 <223> GrB variant C228F

 <400> 57

 Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg Pro Tyr Met Ala
 1 5 10 15

Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg Cys Gly Gly Phe
 20 25 30

Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His Cys Trp Gly Ser
 35 40 45

Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys Glu Gln Glu Pro
 50 55 60

Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro His Pro Ala Tyr
 65 70 75 80

Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu Gln Leu Glu Arg
 85 90 95

Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg Leu Pro Ser Asn
 100 105 110

Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val Ala Gly Trp Gly
 115 120 125

Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu Gln Glu Val Lys
 130 135 140

Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp Leu Arg His Tyr
 145 150 155 160

Tyr Asp Ser Thr Ile Glu Leu Cys Val Gly Asp Pro Glu Ile Lys Lys
 165 170 175

Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Asn Lys Val
 180 185 190

Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly Met Pro Pro Arg
 195 200 205

Ala Phe Thr Lys Val Ser Ser Phe Val His Trp Ile Lys Lys Thr Met
 210 215 220

Lys Arg Tyr
 225